REMARKS

Claims 55-108 were pending in this application when last examined. Claims 55-57, 59-68, 70-71, 75-76, 78, 82-84, 87-88, 90-93, 102, and 104 have been amended, claims 58, 69, 73, 89, 95-101, and 105-108 have been cancelled without prejudice, and new claim 109 has been added. Support for the amendments can be found in the specification, for example, at pages 10 and 13-15, and in the original claims as filed. No new matter has been added.

In response to the Restriction Requirement, Applicants hereby provisionally elect Group I, claims 55-69, drawn to a genetically modified rodent. Note that currently amended claims 55-69 are now directed to a genetically modified mouse. This election is made with traverse.

The Office Action recognizes that the instant application is a 371 National stage application of PCT/NO2004/000397, and thus, PCT rules regarding unity of invention apply.

PCT Rule 13.1 deals with the requirement of unity of invention and states that an international application should relate to only one invention, or if there is more than one invention, that the inclusion of those inventions in one international application is only permitted if all inventions are so linked as to form a single general inventive concept.

PCT Rule 13.2 defines the method for determining whether the requirement of unity of invention is satisfied in respect to a group of inventions claimed in an international application. Unity of invention exists when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding "special technical features." The expression "special technical features" is defined in Rule 13.2 as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art.

In view of the above amendments and the following remarks, the claims of Groups I, II, III and/or V satisfy the requirements of PCT Rule 13.1 and PCT Rule 13.2 for unity of invention.

PRIOR ART

Addressing first the references cited in the Office Action, PERIASAMY et al. discloses that Serca2 plays a central role in cardiomyocyte Ca^{2+} handling and that a reduced level of Serca2 is a factor in heart disease. Based on this, the authors in PERIASAMY expected that homozygous Serca2 mutants would not survive and that it would be necessary to perform the studies on heterozygotes. (See, Abstract, and page 2560, first paragraph of Discussion).

Indeed, VER HEYEN et al. (copy enclosed in the Appendix) also demonstrated that the Serca2a variant is critical for both cardiac development and function and that the Serca2b isoform is not compatible with normal cardiac function.

Thus, in view of the state of the art at the time of invention, one of ordinary skill in the art would expect that a homozygous Serca2 deletion, once induced, would be instantly lethal in adult mice. Such an animal model would obviously serve no purpose. One of ordinary skill would be led away from any such procedure as described in the present application.

Nevertheless, even if one of ordinary skill disregarded the expected obstructions within the field, one would not apply the tamoxifin inducible system presently disclosed. It is well known in the art that tamoxifin inhibits, inter alia, both Ca^{2+} uptake by the cardiac SR and Na^{+} and K^{+} currents in myocytes (see, KARGACIN et al., and HE et al., copies enclosed in the Appendix). Each of these three currents is an important factor in cardiac contractility. The skilled artisan would never apply an induction system that affects the same phenomenon that is to be studied.

Despite the prevailing evidence indicated by the state of the art which would have led away from the present teachings, the applicants have overcome this prejudice and surprisingly found that a homozygous Serca2 deletion, once induced, is not instantly lethal in adult mice.

Group I

Claims 55-69, as currently amended, are directed to a genetically modified mouse having its genomic Serca ATPase gene modified by inserted recombination sites of heterogenous origin, said modification being homozygous.

Group II

Claims 70-86, as currently amended, are directed to an eukaryotic cell, having its genomic Serca ATPase gene modified by inserted recombination sites of heterogenous origin, said modification being homozygous.

In view of the amendments, the claims of Group I (genetically modified mouse) and the claims of Group II (genetically modified eukaryotic cell) share at least one common technical feature that define a contribution in which the claims considered as a whole make over the prior art.

Group III

Claims 87-92, as currently amended, are directed to a gene encoding a Serca ATPase modified by inserted recombination sites, wherein said recombination sites are heterogenous to said gene. Claims 93-94 are directed to a vector comprising a gene encoding a Serca ATPase modified by inserted recombination sites, wherein said recombination sites are heterogenous to said gene.

The Office Action fails to recognize that the claims of Group III are intermediate products of the final products defined in Groups I and II. The chemical structures of the intermediate and final products are technically closely interrelated. The intermediate product incorporates essential structural elements into the final product and the final product is manufactured directly from the intermediate or is separated from it by a small number of intermediates all containing the same essential structural element. Thus, for at least this reason, unity of invention exists regarding the claims of Group III and the claims of Group I and Group II.

Group IV

The claims of Group IV, claims 95-101, have been cancelled.

Group V

Claims 102-108 as currently amended, and new claim 109, are directed to a method for screening a compound or a mixture of compounds for activity against defective Ca^{2+} handling. The method includes:

- inducing expression of the recombinase, and with that inactivation of the Serca ATPase gene, in the mouse according to claim 1;

- administrating the compound or a mixture of compounds to said mouse before and/or after the induced inactivation of the SercaATPase gene; and
- detecting whether the induced defective Ca^{2+} handling is normalized by the administration of said compound or mixture of compounds.

The Office Action recognizes that a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn to: a product, a process specially adapted for the manufacture of said product, and a use of said product (37 CFR 1.475 (b)(3)).

Therefore, because the method of claims 102-109 involves the use of the genetically modified mouse defined in claim 1, unity of invention exists at least regarding the claims of Group V and the claims of Groups I.

CONCLUSION

For all the reasons set forth in the remarks above, Applicants respectfully traverse the Examiner's conclusion of the absence of a special technical feature among any of Groups I-III and V. Applicants submit that the Office Action fails to satisfy the requirements of PCT Rules 13.1 and 13.2. Applicants submit that the present claims define a contribution over the prior art

and that unity of invention among Groups I-III and V should be recognized.

Therefore, all of the pending claims are sufficiently related so as to warrant a search and examination of all the claims in their full scope. Favorable action on the merits is solicited.

Should there be any matters that need to be resolved in the present application the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON

/H. James Voeller/

H. James Voeller, Reg. No. 48,015
209 Madison Street
Suite 500
Alexandria, VA 22314
Telephone (703) 521-2297
Telefax (703) 685-0573
(703) 979-4709

HJV/fb

APPENDIX:

- VER HEYEN et al.
- KARGACIN et al.
- HE et al.